

### **Amendment to Specification**

In the Specification:

Please replace the heading/first paragraph on page 1, line 1 of the application with the following amended paragraph:

#### **CROSS-REFERENCE TO RELATED APPLICATIONS**

[0001] ~~This application~~ This Application, U.S. Serial Number 10/541,182, is a 371 National Stage of International Application No. PCT/US2004/000255 filed on January 7, 2004, which designated the U.S., and which claims the benefit under 35 U.S.C. § 119(e) of U.S. Provisional Application No. 60/438,393 filed on January 7, 2003.

Please delete paragraph [0118] and replace it with the following paragraph:

[0118] Cocoons from ~~Bombyx Mori~~ *Bombyx mori* were boiled for 1 hour in an aqueous solution of 0.02M Na<sub>2</sub>CO<sub>3</sub>, and rinsed with water to extract sericins. Purified silk was solubilized in 9M LiBr solution and dialyzed (Pierce, MWCO 2000 g/mol) against PBS for 1 day and again against 0.1M MES, 0.5 M NaCl, pH 6 buffer for another day. An aliquot of the silk solution was coupled with GRGDS (SEQ ID NO: 7) peptide to obtain RGD-silk. For coupling COOH groups on the silk were activated by reaction with 1-ethyl-3-(dimethylaminopropyl)carbodiimide hydrochloride (EDC)/ N-hydroxysuccinimide (NHS) solution for 15 minutes at room temperature (Sofia et al. 2001. J Biomed Mater Res 54:139-148). To quench the EDC, 70 µl/ml β-mercaptoethanol was added. Then 0.5 g/l peptide was added and left for 2 hours at room temperature. The reaction was stopped with 10 mM hydroxylamine. Silk solutions were dialyzed against 0.1 M 2-(N-morpholino)-ethanesulfonic acid buffer, pH 4.5-5 for 1 day. Silk and Silk-RGD solutions were lyophilized and redissolved in hexafluoro-2-propanol (HFIP) to obtain a 17% (w/v) solution. Granular NaCl was weighed in a Teflon container and silk/HFIP solution was added at a ratio of 20:1 (NaCl/silk). HFIP was allowed to evaporate for 2 days and NaCl/silk blocks were immersed in 90% (v/v) methanol for 30 minutes to induce a protein conformational transition to β-sheet (Nazarov et al. 2003. In Department of Biomedical

Engineering, Medford: Tufts University). Blocks were removed, dried and NaCl was extracted in water for 2 days. Disk shaped scaffolds (5 mm diameter, 2 mm thick) were prepared using a dermal punch (Miltey, Lake Success, NY), and autoclaved.

Please delete paragraph [0142] and replace it with the following paragraph:

[0142] Cocoons from ~~Bombyx Mori~~ *Bombyx mori* (Linne, 1758) were boiled for 1 hour in an aqueous solution of 0.02M Na<sub>2</sub>CO<sub>3</sub>, and rinsed with water to extract sericins. Purified silk was solubilized in 9M LiBr solution and dialyzed (Pierce, Woburn, MA; MWCO 3500 g/mol) against water for 1 day and again against 0.1M MES (Pierce), 0.5 M NaCl, pH 6 buffer for another day. An aliquot of the silk solution was coupled with glycine-arginine-alanine-glycine-aspartate-serine (GRGDS; SEQ ID NO: 7) peptide to obtain RGD-silk. For coupling COOH groups on the silk were activated by reaction with 1-ethyl-3-(dimethylaminopropyl)carbodiimide hydrochloride (EDC)/ N-hydroxysuccinimide (NHS) solution for 15 minutes at room temperature (Sofia et al. 2001. J Biomed Mater Res 54:139-148). To quench the EDC, 70 µl/ml β-mercaptoethanol was added. Then 0.5 g/l peptide was added and left for 2 hours at room temperature. The reaction was stopped with 10 mM hydroxylamine. Silk solutions were dialyzed against water for 2 days. Silk and Silk-RGD solutions were lyophilized and redissolved in hexafluoro-2-propanol (HFIP) to obtain a 17% (w/v) solution. Granular NaCl was weighed in a Teflon container and silk/HFIP solution was added at a ratio of 20:1 (NaCl/silk). HFIP was allowed to evaporate for 2 days and NaCl/silk blocks were immersed in 90% (v/v) methanol for 30 minutes to induce a protein conformational transition to β-sheets (Nazarov et al. 2003. In Department of Biomedical Engineering, Medford: Tufts University). Blocks were removed, dried and NaCl was extracted out in water for 2 days. Disk shaped scaffolds (5 mm diameter, 2 mm thick) were prepared using a dermal punch (Miltey, Lake Success, NY), and autoclaved.

Please delete paragraph [051] and replace it with the following amended paragraph:

[051] Figures 15A-D show µ-CT images taken from collagen (~~16A, 16B~~ 15A, 15B), and silk-RGD scaffolds (~~16C, 16D~~ 15C, 15D). Insert in ~~16C~~ 15C is a magnification from ~~16D~~ 15D. Bar length = 1.1 mm.

Please delete paragraph [052] and replace it with the following amended paragraph:

[052] Figures 16A-L show u-CT images of tissue engineered bone on three silk scaffolds with mean pore sizes of 106 um (~~17A, 17D, 17G~~ 16A, 16D, 16G), 225 um (~~17B, 17E, 17H~~ 16B, 16E, 16H), and 425 um (~~17C, 17F, 17I~~ 16C, 16F, 16I). The first row (~~17A-17C~~ 16A-16C) shows a face view, the second row (~~17D-17F~~ 16D-16F) a lateral view and the third row (~~17G-17I~~ 16G-16I) a magnification of A-C. ~~17J-17L~~ 16-J-16L shows scaffolds prior to tissue culture of a mean pore size of 106 um, 225 um, and 425, um respectively.